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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	11

DATE MAILED: 06/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,261	QUINNAN ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on th cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-22* is/are pending in the application.

4a) Of the above claim(s) *7-15,17-20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6,16 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 and 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant cancelled claim 1 and amended claims 5-9, 12, 16, 17, 19, and 20 in paper no. 10.

Election/Restrictions

It is noted that group IX contains a typo in the restriction requirement. The group contains the subject matter of claim 22, not 21.

Applicant's election with traverse of group I in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the special technical feature of group I is a protein which induces cross-reactive HIV antibodies. Applicant argues that the protein used to induce the production of antibodies group VI and to detect the presence of the antibodies in group VIII. Applicant further argues that groups I and VI are linked to form a single inventive concept.

Applicant's arguments have been considered and are partly persuasive. The special technical feature of group I is the isolated envelope protein, not the induction of antibodies with the protein. However, since claims 5 and 6 of group I indicate an immunological response with the protein, the method of inducing antibodies with the protein of group VI is also related and will be rejoined. However, applicant's arguments are unpersuasive with respect the group VIII since the group is drawn to a second method of using the first product. The teaching of the special technical feature by Haynes et al. in the restriction requirement has broken unity between the inventive concepts linked by the special technical feature. Therefore, the products and methods have been properly separated according to the MPEP § 1850, section A.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-15, 17-20, and 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. Claims 2-6, 16, and 21 are under consideration.

Specification

The disclosure is objected to because of the following informalities: There are two figures labeled Figure 1 and Figure 2 following the claims which appear to illustrate flow charts. There is no brief description for these figures and it is unclear whether these figures are intended to be part of the instant disclosure or not.

Appropriate correction is required.

Sequence Compliance

The specification and the claims are objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific sequences in the specification and the claims. For example, see page 33, Table 3 and the "R2" clone, clade, or subtype in Table 5. In addition, claim 4 recites more than 4 amino acid residues in a sequence and must be appended by a SEQ ID NO. See 37 CFR § 1.821(d) and MPEP § 2422.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6, 16, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is unclear because the metes and bounds of what would be considered a "fragment" of SEQ ID NO: 1 cannot be determined. Are the position numbers corresponding to a certain region, i.e., V3, or can the position numbers correspond to any part of the envelope protein? This rejection affects claims 4-6, 16, and 21.

Claim 4 is vague and indefinite because residues X_1-X_{10} are not adequately described since a non-natural amino acid sequence may include chemicals, enzymes, and/or various other molecules. It cannot be determined what a non-natural amino acid encompasses. Moreover, protein and the "fragment" is indefinite since X_1-X_{10} of each may be anything or non-existent. Since an envelope protein of HIV would only comprise natural amino acids, it cannot be discerned how an envelope protein or fragment would comprise anything other than amino acid residues. This rejection affects claims 5, 6, 16, and 21.

Claim 5, 6, and 16 are unclear because the claims encompass a "fragment of any one of claims 2-4". Claims 3 and 4 recite fragments. Therefore, are claims 5, 6, and 16 drawn to fragments of the fragments in claims 3 and 4?

Claim 21 is vague and indefinite because the amino acid sequences of claims 3 and 4 are not definite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6, 16, and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 3 is drawn to an isolated HIV protein or fragment comprising specific residues at certain positions. However, it cannot be determined by the claim whether a particular region of the envelope protein is being claimed or where in an envelope protein the sequence is required to be located. The disclosure does not teach any fragment of an HIV envelope protein that may have these regions except V3. Claim 4 is drawn to the V3 region of an HIV envelope protein or any fragment thereof having an undefined sequence. The specification does not teach that every possible sequence comprising PM X_1-X_{10}Q would be specifically derived from the V3 region of an HIV envelope protein, nor does the specification teach molecules that are not natural amino acid sequences as part of the V3 region, or how the skilled artisan could recognize an HIV envelope protein or fragment that comprises non-natural amino acids. Claims 5, 6, 16, and 21 encompass fragments of the fragments of claims 3 and 4. The specification does not teach the structure or function of such derivatives or cyclic peptides of fragments or fragments of fragments. Therefore, it is determined that the specification does not convey possession of the fragments, fragments of fragments, or all of the possible cyclic peptides encompassed by the claims.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is drawn to an HIV vaccine comprising an HIV envelope protein encoding SEQ ID NO: 1 or fragment thereof. As discussed above, the instant disclosure fails to

adequately describe all of the possible variants of SEQ ID NO: 1 claimed and the skilled artisan would be unable to make or recognize all of the possible fragments in the art. One of skilled in the art would doubt the efficacy of the claimed vaccine with the instant protein or any fragment thereof because there is no teaching that there would be divergent cross-reactivity between the different subgroups and clades. Lukashov et al. (AIDS Research and Human Retroviruses. 1996; 12 (10): 951-953) teaches the various sequences in the HIV envelope V3 region, which includes the instantly claimed phenotype, see the sequence alignment provided and reference sequence "SR923572" in Figure 1. Lukashov et al. sequences 44 individuals in this region and only one is found to have the instant sequence. Therefore, this sequence does not representative in a large number of subjects and the skilled artisan would doubt the cross-reactivity of the instant sequence with other serum samples derived from different strain of HIV. Therefore, the comparative neutralization of different sera with R2 and envelopes with other diverse phenotypes in example 4 of the disclosure is not indicative of the type of response to the protein once administered due to diverse variation of HIV sequences. Hypervariability of sequences among the different HIV strains is a well-recognized concern in the HIV art; see the teachings of Korber et al. (British Medical Bulletin. 2001; 58: 19-42) as a general review in the art. The teachings of Kelleher et al. (AIDS Research and Human Retroviruses. 1997; 13 (1): 29-32) provide further evidence that the instant protein or fragments would not induce a protective immune response. Kelleher et al. teaches poor immune response following administration of a V3 peptide and an adjuvant to 24 individuals. The working examples do not provide evidence that the instant composition provides protection. There is currently no animal model for HIV, see the teachings of Klein et al. (Clinical Therapeutics. 2000; 22 (3): 295-314) on pages 304-305. Therefore, the

neutralization assays in mice immunized with full-length R2 and R2 fragments in example 9 of the specification does not indicate the applicability to humans. The skilled artisan would be unable to predict the response or effectiveness of the instantly claimed protein. In conclusion, the instant specification does not address or remedy the concerns in the art.

Therefore, due to the scope of the claims drawn to a vaccine with SEQ ID NO: 2 and any fragment thereof with no defined structure, the lack of predictability in the HIV vaccine art, and the lack of data in the disclosure drawn to cross-neutralization among all of the hypervariable sequences among the various HIV strains, it is determined that undue experimentation would be required of the skilled artisan to make or use the instant vaccine.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Sala et al. (Journal of Virology. 1994; 68 (8): 5280-5283).

The claim is drawn to an isolated HIV envelope protein comprising the amino acid sequence of SEQ ID NO: 1.

Sala et al. teaches isolating and amplifying sequences from the V3 region of HIV and determining the amino acids differing from the consensus V3 sequence, which are contained within 297 to 335 position numbers of V3, see the paragraph bridging pages 5281-5282 and

Figure 2. Although Sala et al. does not teach the entire envelope protein amino acid sequence, this sequence would be an inherent property of the envelope protein sequenced by the reference.

Claims 3 and 4 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the sequence alignment of Sala et al. (SPTREMBL_17 database; Accession No: Q78039; November, 1996; from J. Virol.; 68: 5280-5283) or the sequence alignment of Lukashov et al. (SPTREMBL_17 database; Accession No: Q69692; 1996; from AIDS Research and Human Retroviruses; 12: 951-953) in the alternative.

The claims are drawn to an isolated HIV envelope protein or fragment thereof comprising specific amino acid residues at specific cites.

Sala et al. or Lukashov et al. clearly anticipate the claimed sequences. The sequence alignments of Sala et al. or Lukashov et al. teach residues 310 to 327 of instantly claimed SEQ ID NO: 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sala et al. supra.

The claim is drawn to an immunogenic composition comprising an isolated envelope protein encoding SEQ ID NO: 1 or a fragment thereof and a pharmaceutical carrier.

See the teachings of Sala et al. above. The reference teaches amplifying DNA, cloning, and determining amino acid residue sequences, see the first paragraph on page 5281 and the

paragraph bridging pages 5281-5282. The buffer used conventionally in the art to preserve DNA, clones, and the envelope proteins would be a pharmaceutically acceptable carrier.

Claims 6 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sala et al. as applied to claims 2-4 above, and further in view of Haynes et al. (US 5,019,387).

The claims are drawn to an immunogenic composition comprising the isolated HIV envelope protein or fragment and a method of generating antibodies in a mammal by administering the composition.

See the teachings of Sala et al. above. Sala et al. does not teach generating antibodies with the HIV envelope protein or fragment.

However, Haynes et al. teaches an immunogenic conjugate comprising an HIV envelope glycoprotein that induces antibodies, see claim 4.

One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the envelope sequences of Sala et al. to expand the number of antigenic determinants in the conjugate of Haynes et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because Haynes et al. induces antibodies with HIV envelope proteins with a hydrophilic carrier and Sala et al. teaches different sequences of HIV envelope proteins. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley/SAF
June 10, 2002

JAMES HOUSEL 6/17/02
SUPERVISORY PATENT EXAMINER
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